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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/601,968

06/23/2003

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AHPWA23AUSA

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01/17/2006

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EXAMINER

KWON, BRIAN YONG S

ART UNIT

PAPER NUMBER

1614

DATE MAILED: 01/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/601,968	Applicant(s) FENSOME ET AL.	
	Examiner Brian S. Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 4,6,8 and 10-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,7 and 9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants Response to Restriction/Election of Species Requirement Acknowledged

1. In response to the Restriction requirement mailed September 28, 2005, the Applicant elected without traverse the Group II(a) claims 1-12.
2. Acknowledgment is made of applicant's election of the 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3, 1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile as the elected species in response to the Examiner's telephonic Election of Species requirement. During a telephone conversation with Cathy A. Kodroff made on January 10, 2006 a provisional election was made to prosecute the 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3, 1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile as the elected species. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-3, 5, 7 and 9 read on the elected species. Accordingly, claims 4, 6, 8 and 10-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The instant claims 1-7 and 10-12 are generic to a plurality of disclosed patentably distinct species comprising the various groups that are embraced by the laundry lists of R1, R2, R3, R4, R5 and Q1 variables. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

With the election of a specific exemplified compound, a generic concept will be identified by the examiner as the inventive group for examination.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the

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examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. Currently, claims 1-3, 5, 7 and 9 are pending for prosecution on the merits of the case.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5, 7 and 9 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for treating acne and/or hirsutism with 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile or its pharmaceutically acceptable salt, does not reasonably provide enablement for treating said condition with “a compound of formula I...or a pharmaceutically acceptable salt, tautomer, metabolite or prodrug thereof”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

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The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The invention relates to a method of treating acne or hirsutism comprising administering a compound of formula I, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

The compounds of the inventions are recognized as progesterone receptor modulator or androgen/progesterone receptor modulator.

The relative skill of those in the art of pharmaceuticals or the unpredictability of the pharmaceutical is very high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the full scope of the claimed compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The scope of the claims are very broad due to the vast number possible compounds represented by compound of Formula I or a pharmaceutical acceptable salt, tautomer, metabolite, or prodrug thereof.

The specification (Examples 8 and 9) discloses the results of study showing the efficacy of 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile in treating acne or hirsutism as the sole example. As discussed above, there is no data or any competent evidence or disclosed tests that are highly predictive for the claimed utility by all of the claimed compounds embraced by the instant claims.

The specification provides insufficient guidance or information allowing the skill artisan to determine which compound(s) of the claimed compounds represented by the formula I would be able to accomplish the desired result of the claimed invention without undue amount of experimentation. Furthermore, the specification does not provide sufficient guidance allowing the skilled artisan to determine what is “metes and bounds” of “tautomer, metabolite or prodrug thereof”. The instantly claimed “tautomer, metabolite or prodrug” necessitates an exhaustive search for the embodiments suitable to practice the claimed invention.

As discussed above, the specification fails to provide sufficient guidance or information in the way of enablement for the full scope of all compounds of formula I or their tautomers, metabolites or prodrugs that are potentially suitable for the invention work similarly as to the 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile.

Since the efficacy of the genus of compounds represented by the formula I or their tautomers, metabolites or prodrugs in treating acne or hirsutism cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the

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above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 5, 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The independent claim 1 recites that R5 is selected from the group consisting of (i) and (ii). However, there is insufficient antecedent basis for "(ii)" in the claim. This inconsistency leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

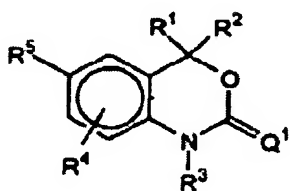
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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-3, 5, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (WO 00/66581) in view of Zhi et al. (US 6566372 B1).

Zhang teaches the use of compounds represented by the formula I,



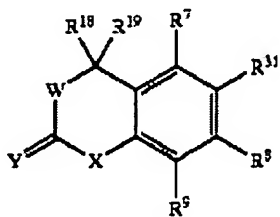
I

such as 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-zH-3,l-

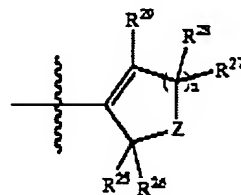
benzoxazin-6-yl)-l-methyl-l H-pyrrole-2-carbonitrile (Example 62) as progesterone receptor antagonist that is useful in the treatment of fibrosis, endometriosis, breast, uterine, ovarian and prostate cancer, and post menopausal hormone replacement therapy.

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Zhi teaches the use of compounds represented by the formula XIII,



wherein W and X include O; Y includes S; R7, R8 and R9



include H; R18 and R19 include hydrogen; and R31 include

, as androgen

and progesterone receptor modulator (agonist and antagonists) that is useful in the treatment of various disease including hirsutism and acne. Scheme XXII and Scheme XXIV (column 67, line 10 thru column 71, line 50) in Zhi disclose the claimed cyclothiocarbamate derivatives (which reads on the genus of the formula I compounds), for example Structure 117 when Y=S.

The claimed invention differs from the Zhang by having CN and methyl substituents at pyrrole ring in the 1, 2 position respectively. One having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that such substitution would not significantly alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. Thus, one would have been motivated to combine these references and make the modification to arrive at the claimed utility because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Conclusion

6. No Claim is allowed.

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7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

A handwritten signature in black ink, appearing to be 'B. Kwon', with a long horizontal line extending to the right.